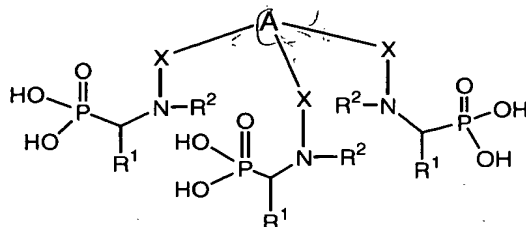
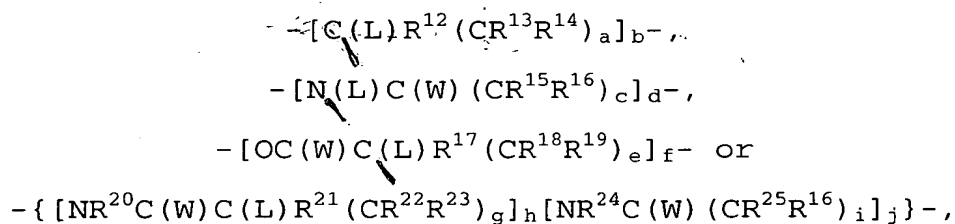


CLAIMS:

1. A tripodal polyaminophosphonate chelant having the formula:



and pharmaceutically acceptable salts thereof, wherein A is selected from the group consisting of CR^3 , SiR^3 , GeR^3 , N, P, $P=O$, $P=S$, As, $As=O$, and a macrocyclic group having the formula:



wherein a is an integer selected from 1 to 3;

b is an integer selected from 3 to 5;

c is an integer selected from 1 to 3;

d is an integer selected from 3 or 4;

e is an integer selected from 1 to 3;

f is an integer selected from 3 or 4;

g is an integer selected from 1 to 3;

h is an integer selected from 3 or 4;

i is an integer selected from 1 to 3;

j is an integer selected from 0 to 3;

L is a direct bond to X;

5 W is H₂ or O;

R¹ is (CR⁴R⁵)_nR⁶, wherein n is an integer selected from 0 to 3;

10 R², R³, R⁴, R⁵ and R⁶ are independently selected from the group consisting of H, C₁-C₁₀ alkyl substituted with 0-5 R⁷, C₁-C₁₀ fluoroalkyl substituted with 0-5 R⁷, C₂-C₁₀ alkenyl substituted with 0-5 R⁷, C₂-C₁₀ fluoroalkenyl substituted with 0-5 R⁷, aryl substituted with 0-5 R⁷, heteroaryl substituted with 0-5 R⁷ and 15 fluoroaryl substituted with 0-5 R⁷; or R⁴ and R⁵ may be taken together to form a C₃-C₁₀ cycloalkyl or C₃-C₁₀ cycloalkenyl optionally interrupted with C(O)NH, NH, NHC(O), NHC(O)NH, NHC(S)NH, O, S, S(O), S(O)₂, P(O)(OR⁸), P(O)(OR⁸)O, P(O)(NHR⁷)O, or to form an aryl 20 substituted with 0-5 R⁷, a fluoroaryl substituted with 0-5 R⁷ or an N-containing heterocycle substituted with 0-5 R⁷.

R⁷ is selected from the group consisting of H, OH, C(=O)R⁸, C(=O)OR⁸, C(=O)NR⁸, (PO(OR⁸))₂ and S(O)₂OR⁸;

25 R⁸ is selected from the group consisting of H, C₁-C₆ alkyl, C₃-C₆ cycloalkyl, C₁-C₆ fluoroalkyl, C₁-C₆ alkenyl, C₃-C₆ cycloalkyl, C₁-C₆ fluoroalkenyl, benzyl, fluorobenzyl, phenyl and fluorophenyl;

30 X is selected from the group consisting of (CR⁹R¹⁰)_m, NR¹¹, and O(CR⁹R¹⁰)_m, wherein m is an integer selected from 1 to 3, provided that when A is N or - [N(L)C(W)(CR¹⁵R¹⁶)_c]_d-, X is (CR⁹R¹⁰)_m;

R^9 , R^{10} and R^{11} are independently selected from the group consisting of H, C_1 - C_{10} alkyl substituted with 0-5 R^7 , C_1 - C_{10} fluoroalkyl substituted with 0-5 R^7 , C_2 - C_{10} alkenyl substituted with 0-5 R^7 , C_2 - C_{10} fluoroalkenyl substituted with 0-5 R^7 , aryl substituted with 0-5 R^7 and fluoroaryl substituted with 0-5 R^7 ; or R^9 and R^{10} may be taken together to form a C_3 - C_{10} cycloalkyl or C_3 - C_{10} cycloalkenyl optionally interrupted with $C(O)NH$, NH , $NHC(O)$, $NHC(O)NH$, $NHC(S)NH$, O , S , $S(O)$, $S(O)_2$, $P(O)(OR^8)$, $P(O)(OR^7)O$, $-P(O)(NHR^7)O$, or to form an aryl substituted with 0-5 R^8 or fluoroaryl substituted with 0-5 R^8 ; and

R^{12} , R^{13} , R^{14} , R^{15} , R^{16} , R^{17} , R^{18} , R^{19} , R^{20} , R^{21} , R^{22} , R^{23} , R^{24} , R^{25} , and R^{26} are independently selected at each occurrence from the group consisting of H, C_1 - C_6 alkyl, C_3 - C_6 cycloalkyl, C_1 - C_6 fluoroalkyl, C_1 - C_6 alkenyl, C_3 - C_6 cycloalkenyl, C_1 - C_6 fluoroalkenyl, benzyl, fluorobenzyl, phenyl and fluorophenyl.

2. A tripodal polyaminophosphonate chelant according to claim 1, wherein:

A is selected from the group consisting of CR^3 , N and $P=O$;

R^1 is $(CH_2)_nR^6$;

R^2 , R^3 and R^6 are independently selected from the group consisting of H, C_1 - C_{10} alkyl substituted with 0-2 R^7 , C_1 - C_{10} fluoroalkyl substituted with 0-2 R^7 , C_2 - C_{10} alkenyl substituted with 0-2 R^7 , C_2 - C_{10} fluoroalkenyl substituted with 0-2 R^7 , aryl substituted with 0-2 R^7 , fluoroaryl substituted with 0-2 R^7 and heteroaryl substituted with 0-2 R^7 ;

X is selected from the group consisting of $(CH_2)_m$, NR^{11} and $O(CR^9R^{10})_m$, wherein m is an integer selected from 1 to 3, provided that when A is N, X is $(CH_2)_m$; and

R^{11} is selected from the group consisting of H, C_1 - C_{10} alkyl substituted with 0-2 R^7 , C_1 - C_{10} fluoroalkyl substituted with 0-2 R^7 , C_2 - C_{10} alkenyl substituted with 0-2 R^7 , C_2 - C_{10} fluoroalkenyl substituted with 0-2 R^7 , aryl substituted with 0-2 R^7 and fluoroaryl substituted with 0-2 R^7 .

10

3. A tripodal polyaminophosphonate chelant according to claim 2, wherein:

A is CR^3 or N;

n is 0 or 1;

15

R^2 and R^3 are independently selected from the group consisting of H, C_1 - C_{10} alkyl, C_1 - C_{10} fluoroalkyl, C_2 - C_{10} alkenyl, C_2 - C_{10} fluoroalkenyl, aryl and fluoroaryl;

R^6 is an aryl or heteroaryl group substituted with 0-2 R^7 ;

20

R^7 is selected from the group consisting of H, OH, $C(=O)OH$, $C(=O)NH_2$, $PO(OH)_2$ and $S(O)_2OH$; and

X is $(CH_2)_m$, wherein m is 1 or 2.

4. A tripodal polyaminophosphonate chelant according to claim 3, wherein:

25

A is CR^3 or N;

R^2 is H;

R^3 is selected from the group consisting of H, C_1 - C_{10} alkyl and C_1 - C_{10} aryl;

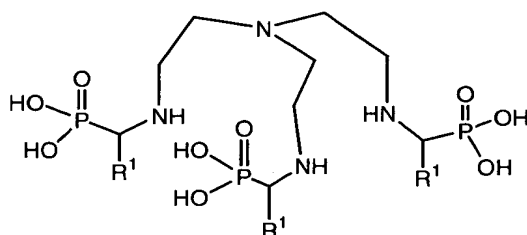
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R^6 is an aryl or heteroaryl group substituted with 0-2 R^7 ;

R^7 is selected from the group consisting of H, OH, $C(=O)OH$, $PO(OH)_2$ and $S(O)_2OH$; and

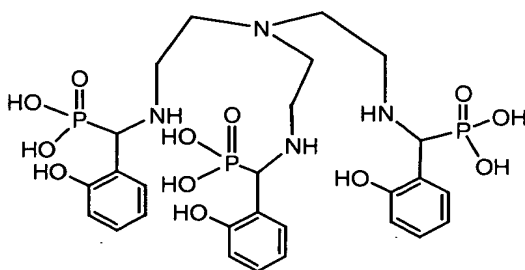
X is $(CH_2)_m$, wherein m is 1 or 2.

- 5 5. A tripodal polyaminophosphonate chelant according to claim 4, having the formula:



- 10 wherein R^1 is selected from the group consisting of phenyl, benzyl, imidazolyl, pyridyl and thiophenyl, each substituted with 0-2 OH.

- 15 6. A tripodal polyaminophosphonate chelant according to claim 5, having the formula:



- 20 7. The tripodal polyaminophosphonate chelant of claim 1, wherein the phosphorous atoms in said chelant comprise ^{32}P .

8. A radiopharmaceutical compound comprising a tripodal polyaminophosphonate chelant according to claim 1, chelated with a radionuclide selected from the group consisting of ^{52m}Mn , ^{52}Fe , ^{55}Co , ^{64}Cu , ^{67}Cu , ^{67}Ga , ^{68}Ga , ^{90}Y , ^{94m}Tc , ^{99m}Tc , ^{105}Rh , ^{109}Pd , ^{111}In , ^{117m}Sn , ^{149}Pr , ^{153}Sm , ^{159}Gd , ^{166}Ho , ^{169}Yb , ^{177}Lu , ^{186}Re , ^{188}Re , ^{203}Pb , ^{211}Pb , and ^{212}Bi .

9. A radiopharmaceutical compound according to claim 8, wherein:

A is selected from the group consisting of CR^3 , N and $\text{P}=\text{O}$;

R^1 is $(\text{CH}_2)_n\text{R}^6$;

R^2 , R^3 and R^6 are independently selected from the group consisting of H, $\text{C}_1\text{-C}_{10}$ alkyl substituted with 0-2 R^7 , $\text{C}_1\text{-C}_{10}$ fluoroalkyl substituted with 0-2 R^7 , $\text{C}_2\text{-C}_{10}$ alkenyl substituted with 0-2 R^7 , $\text{C}_2\text{-C}_{10}$ fluoroalkenyl substituted with 0-2 R^7 , aryl substituted with 0-2 R^7 , fluoroaryl substituted with 0-2 R^7 and heteroaryl substituted with 0-2 R^7 ;

X is selected from the group consisting of $(\text{CR}^9\text{R}^{10})_m$, NR^{11} , and $\text{O}(\text{CR}^9\text{R}^{10})_m$, wherein m is an integer selected from 1 to 3, provided that when A is N, X is $(\text{CR}^9\text{R}^{10})_m$;

R^{11} is selected from the group consisting of H, $\text{C}_1\text{-C}_{10}$ alkyl substituted with 0-2 R^7 , $\text{C}_1\text{-C}_{10}$ fluoroalkyl substituted with 0-2 R^7 , $\text{C}_2\text{-C}_{10}$ alkenyl substituted with 0-2 R^7 , $\text{C}_2\text{-C}_{10}$ fluoroalkenyl substituted with 0-2 R^7 , aryl substituted with 0-2 R^7 and fluoroaryl substituted with 0-2 R^7 .

10. A radiopharmaceutical compound according to claim 9, wherein:

A is CR^3 or N;

n is 0 or 1;

5 R^2 and R^3 are independently selected from the group consisting of H, C_1 - C_{10} alkyl, C_1 - C_{10} fluoroalkyl, C_2 - C_{10} alkenyl, C_2 - C_{10} fluoroalkenyl, aryl and fluoroaryl;

R^6 is an aryl or heteroaryl group substituted with 0-2 R^7 ;

10 R^7 is selected from the group consisting of H, OH, $C(=O)OH$, $C(=O)NH_2$, $PO(OH)_2$ and $S(O)_2OH$; and

X is $(CH_2)_m$, wherein m is 1 or 2.

11. A radiopharmaceutical compound according to claim 10, wherein:

A is CR^3 or N;

R^2 is H;

R^3 is selected from the group consisting of H, C_1 - C_{10} alkyl and C_1 - C_{10} aryl;

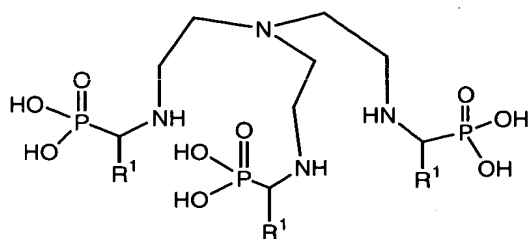
20 R^6 is an aryl or heteroaryl group substituted with 0-2 R^7 ;

R^7 is selected from the group consisting of H, OH, $C(=O)OH$, $PO(OH)_2$ and $S(O)_2OH$; and

X is $(CH_2)_m$, wherein m is 1 or 2.

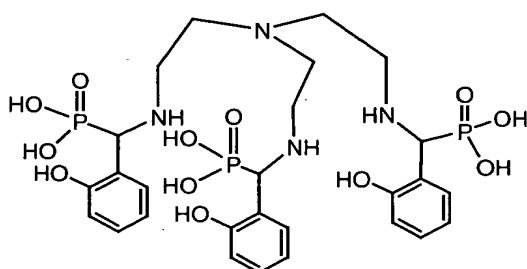
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12. A radiopharmaceutical compound according to claim 11, having the formula:



wherein R^1 is selected from the group consisting of phenyl, benzyl, imidazolyl, pyridyl and thiophenyl, each substituted with 0-2 OH.

13. A radiopharmaceutical compound according to claim 12, having the formula:



10

14. An MRI contrast agent comprising a tripodal polyaminophosphonate chelant according to claim 1, chelated with a paramagnetic metal ion of atomic number 21-29, 42-44 or 58-70.

15. An MRI contrast agent according to claim 14, wherein:

A is selected from the group consisting of CR^3 , N and $P=O$;

20 R^1 is $(CH_2)_nR^6$,

R^2 , R^3 and R^6 are independently selected from the group consisting of H, C_1 - C_{10} alkyl substituted with 0-2

R^7 , C_1 - C_{10} fluoroalkyl substituted with 0-2 R^7 , C_2 - C_{10} alkenyl substituted with 0-2 R^7 , C_2 - C_{10} fluoroalkenyl substituted with 0-2 R^7 , aryl substituted with 0-2 R^7 , fluoroaryl substituted with 0-2 R^7 and heteroaryl substituted with 0-2 R^7 ;

X is selected from the group consisting of $(CR^9R^{10})_m$, NR^{11} , and $O(CR^9R^{10})_m$, wherein m is an integer selected from 1 to 3, provided that when A is N, X is $(CR^9R^{10})_m$;

R^{11} is selected from the group consisting of H, C_1 - C_{10} alkyl substituted with 0-2 R^7 , C_1 - C_{10} fluoroalkyl substituted with 0-2 R^7 , C_2 - C_{10} alkenyl substituted with 0-2 R^7 , C_2 - C_{10} fluoroalkenyl substituted with 0-2 R^7 , aryl substituted with 0-2 R^7 and fluoroaryl substituted with 0-2 R^7 .

16. An MRI contrast agent according to claim 15, wherein:

A is CR^3 or N;

n is 0 or 1;

R^2 and R^3 are independently selected from the group consisting of H, C_1 - C_{10} alkyl, C_1 - C_{10} fluoroalkyl, C_2 - C_{10} alkenyl, C_2 - C_{10} fluoroalkenyl, aryl and fluoroaryl;

R^6 is an aryl or heteroaryl group substituted with 0-2 R^7 ;

R^7 is selected from the group consisting of H, OH, $C(=O)OH$, $C(=O)NH_2$, $PO(OH)_2$ and $S(O)_2OH$; and

X is $(CH_2)_m$, wherein m is 1 or 2.

17. An MRI contrast agent according to claim 16, wherein:

A is CR^3 or N;

R^2 is H;

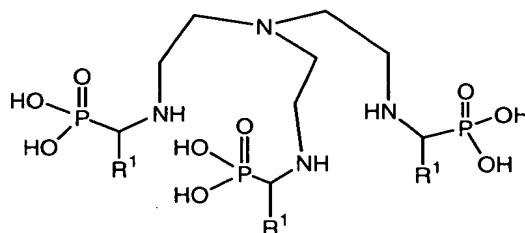
R^3 is selected from the group consisting of H, C_1 - C_{10} alkyl and C_1 - C_{10} aryl;

R^6 is an aryl or heteroaryl group substituted with
5 0-2 R^7 ;

R^7 is selected from the group consisting of H, OH, $C(=O)OH$, $PO(OH)_2$ and $S(O)_2OH$; and

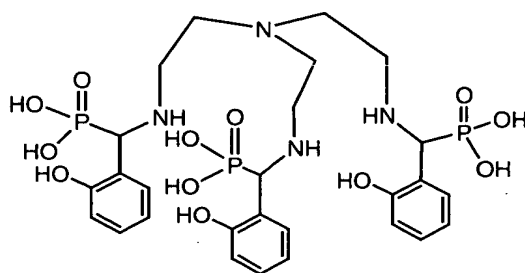
X is selected from: $(CH_2)_m$, wherein m is 1 or 2.

10 18. An MRI contrast agent according to claim 17,
wherein said tripodal polyaminophosphonate chelant has
the formula:



15 wherein R^1 is selected from the group consisting of
phenyl, benzyl, imidazolyl, pyridyl and thiophenyl, each
substituted with 0-2 OH.

20 19. An MRI contrast agent according to claim 18,
wherein said tripodal polyaminophosphonate chelant has
the formula:



20. An X-ray or CT contrast agent comprising a tripodal polyaminophosphonate chelant according to claim 1, chelated with a heavy metal ion of atomic number 21-31, 39-50, 56-80, 82, 83 or 90.

21. An X-ray or CT contrast agent according to claim 20, wherein:

A is selected from the group consisting of CR^3 , N and $P=O$;

R^1 is $(CH_2)_nR^6$;

R^2 , R^3 and R^6 are independently selected from the group consisting of H, C_1 - C_{10} alkyl substituted with 0-2 R^7 , C_1 - C_{10} fluoroalkyl substituted with 0-2 R^7 , C_2 - C_{10} alkenyl substituted with 0-2 R^7 , C_2 - C_{10} fluoroalkenyl substituted with 0-2 R^7 , aryl substituted with 0-2 R^7 , fluoroaryl substituted with 0-2 R^7 and heteroaryl substituted with 0-2 R^7 ;

X is selected from the group consisting of $(CR^9R^{10})_m$, NR^{11} , and $O(CR^9R^{10})_m$, wherein m is an integer selected from 1 to 3, provided that when A is N, X is $(CR^9R^{10})_m$;

R^{11} is selected from the group consisting of H, C_1 - C_{10} alkyl substituted with 0-2 R^7 , C_1 - C_{10} fluoroalkyl substituted with 0-2 R^7 , C_2 - C_{10} alkenyl substituted with 0-2 R^7 , C_2 - C_{10} fluoroalkenyl substituted with 0-2 R^7 ,

aryl substituted with 0-2 R^7 and fluoroaryl substituted with 0-2 R^7 .

22. An X-ray or CT contrast agent according to claim 21, wherein:

A is CR^3 or N;

n is 0 or 1;

R^2 and R^3 are independently selected from the group consisting of H, C_1 - C_{10} alkyl, C_1 - C_{10} fluoroalkyl, C_2 - C_{10} alkenyl, C_2 - C_{10} fluoroalkenyl, aryl and fluoroaryl;

R^6 is an aryl or heteroaryl group substituted with 0-2 R^7 ;

R^7 is selected from the group consisting of H, OH, $C(=O)OH$, $C(=O)NH_2$, $PO(OH)_2$ and $S(O)_2OH$; and

X is $(CH_2)_m$, wherein m is 1 or 2.

23. An X-ray or CT contrast agent according to claim 22, wherein:

A is CR^3 or N;

R^2 is H;

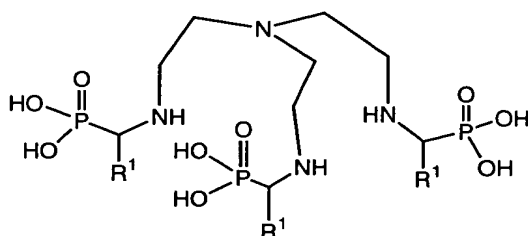
R^3 is selected from the group consisting of H, C_1 - C_{10} alkyl and C_1 - C_{10} aryl;

R^6 is an aryl or heteroaryl group substituted with 0-2 R^7 ;

R^7 is selected from the group consisting of H, OH, $C(=O)OH$, $PO(OH)_2$ and $S(O)_2OH$; and

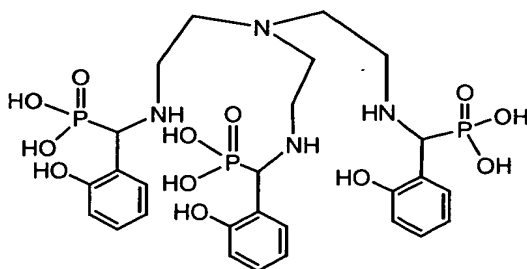
X is selected from: $(CH_2)_m$, wherein m is 1 or 2.

24. An X-ray or CT contrast agent according to claim 23, wherein said tripodal polyaminophosphonate chelant has the formula:



wherein R^1 is selected from the group consisting of phenyl, benzyl, imidazolyl, pyridyl and thiophenyl, each substituted with 0-2 OH.

25. An X-ray or CT contrast agent according to claim 24, wherein said tripodal polyaminophosphonate chelant has the formula:



26. A radiopharmaceutical composition for treating bone disorders that benefit from the delivery of cytotoxic doses of radiation to the bone tissues of a patient in need thereof, comprising a therapeutically effective amount of the tripodal poly-aminophosphonate chelant of claim 7 and a pharmaceutically acceptable carrier.

27. A method for treating bone disorders that benefit from the delivery of cytotoxic doses of radiation to the bone tissues of a patient in need thereof, comprising administering to said patient an effective amount of the radiopharmaceutical composition of claim 26.

28. The method of claim 27, wherein said method comprises relieving bone pain, suppressing bone marrow or treating bone cancer.

29. The method of claim 28, wherein said method comprises treating bone cancer.

30. The method of claim 29, wherein the bone cancer comprises a primary tumor.

31. The method of claim 29, wherein the bone cancer tumor comprises a secondary tumor.

20

32. A composition for radioactive imaging comprising an effective amount of the radiopharmaceutical compound of claim 8 and a pharmaceutically acceptable carrier, wherein the radio-nuclide is selected from the group consisting of ^{52m}Mn , ^{52}Fe , ^{55}Co , ^{64}Cu , ^{60}Cu , ^{62}Cu , ^{67}Ga , ^{68}Ga , ^{94m}Tc , ^{99m}Tc , and ^{111}In .

33. A method for radioactive imaging comprising administering to a patient to be imaged sufficiently in advance thereto an effective amount of the radioactive imaging composition of claim 32.

34. A method according to claim 33, wherein said method is for imaging bone metastases, bone disorders, myocardial infarction, infarctions of the spleen and
5 bowel, inflammatory bowel disease, radiation injury and metastatic calcification.

35. A method according to claim 33, wherein said imaging method is gamma scintigraphy or positron-
10 emission tomography.

36. A composition for X-ray imaging comprising an effective amount of the contrast agent of claim 20 and a pharmaceutically acceptable carrier.
15

37. A method for X-ray imaging comprising administering to a patient to be imaged sufficiently in advance thereof an effective amount of the X-ray imaging composition of claim 36.
20

38. A method according to claim 37, wherein said method is for imaging bone metastases, bone disorders, myocardial infarction, infarctions of the spleen and bowel, inflammatory bowel disease, radiation injury and
25 metastatic calcification.

39. A method according to claim 37, wherein said X-ray imaging method is CT imaging.

40. A composition for magnetic resonance imaging comprising an effective amount of the contrast agent of claim 14 and a pharmaceutically acceptable carrier.

5 41. A method for magnetic resonance imaging comprising administering to a patient to be imaged sufficiently in advance thereof an effective amount of the magnetic resonance imaging composition of claim 40.

10 42. A method according to claim 41, wherein said method is for imaging bone metastases, bone disorders, myocardial infarction, infarctions of the spleen and bowel, inflammatory bowel disease, radiation injury and metastatic calcification.

15 43. A pharmaceutical composition for treating heavy metal toxicity in a patient in need thereof, comprising a therapeutically effective amount of the tripodal polyaminophosphonate chelant of claim 1 and a
20 pharmaceutically acceptable carrier.

25 44. A method for treating heavy metal toxicity in a patient in need thereof, comprising administering to said patient a therapeutically effective amount of the pharmaceutical composition of claim 43.

30 45. A radiopharmaceutical treatment kit comprising: a sterile, non-pyrogenic formulation comprising a radiopharmaceutical composition according to claim 26, a pH 3-9 buffering agent and optionally one or more additives selected from the group consisting of ancillary ligands, reducing agents, transfer ligands,

buffers, lyophilization aids, stabilization aids, solubilization aids, bacteriostats and equipment for administering said composition.

- 5 46. The treatment kit of claim 45, wherein said formulation is in the form of a sterile solution or lyophilized solid.

- 10 47. A diagnostic kit comprising: a sterile, non-pyro-genic formulation comprising a radiopharmaceutical composition according to claim 32, a pH 3-9 buffering agent and optionally one or more additives selected from the group consisting of ancillary ligands, reducing agents, transfer ligands, buffers, lyophilization aids, stabilization aids, solubilization aids, bacteriostats and equipment for administering said composition.

- 20 48. The diagnostic kit of claim 47, wherein said formulation is in the form of a sterile solution or lyophilized solid.

- 25 49. A diagnostic kit comprising: a sterile, non-pyro-genic formulation comprising an X-ray imaging composition according to claim 36, a pH 3-9 buffering agent and optionally one or more additives selected from the group consisting of ancillary ligands, reducing agents, transfer ligands, buffers, lyophilization aids, stabilization aids, solubilization aids, bacteriostats and equipment for administering said composition.

50. The diagnostic kit of claim 49, wherein said formulation is in the form of a sterile solution or lyophilized solid.

5 51. A diagnostic kit comprising: a sterile,
non-pyro-genic formulation comprising a magnetic
resonance imaging composition according to claim 40, a
pH 3-9 buffering agent and optionally one or more
additives selected from the group consisting of
10 ancillary ligands, reducing agents, transfer ligands,
buffers, lyophilization aids, stabilization aids,
solubilization aids, bacteriostats and equipment for
administering said composition.

15 52. The diagnostic kit of claim 51, wherein said
formulation is in the form of a sterile solution or
lyophilized solid.

20 53. A radiopharmaceutical composition for treating
bone disorders that benefit from the delivery of
cytotoxic doses of radiation to the bone tissues of a
patient in need thereof, comprising a therapeutically
effective amount of the radiopharmaceutical compound of
claim 8 and a pharmaceutically acceptable carrier.

25

54. A method for treating bone disorders that
benefit from the delivery of cytotoxic doses of
radiation to the bone tissues of a patient in need
thereof, comprising administering to said patient an
30 effective amount of the radiopharmaceutical composition
of claim 53.

55. The method of claim 54, wherein said method comprises relieving bone pain, suppressing bone marrow or treating bone cancer.

5 56. The method of claim 55, wherein said method comprises treating bone cancer.

10 57. The method of claim 56, wherein the bone cancer comprises a primary tumor.

58. The method of claim 56, wherein the bone cancer tumor comprises a secondary tumor.

15 59. A radiopharmaceutical treatment kit comprising: a sterile, non-pyrogenic formulation comprising a radiopharma-ceutical composition according to claim 53, a pH 3-9 buffer-ing agent and optionally one or more additives selected from the group consisting of ancillary ligands, reducing agents, transfer ligands, 20 buffers, lyophilization aids, stabiliza-tion aids, solubilization aids, bacteriostats and equipment for administering said composition.

25 60. The treatment kit of claim 59, wherein said formulation is in the form of a sterile solution or lyophilized solid.